Post-liver transplantation bile leaks and strictures

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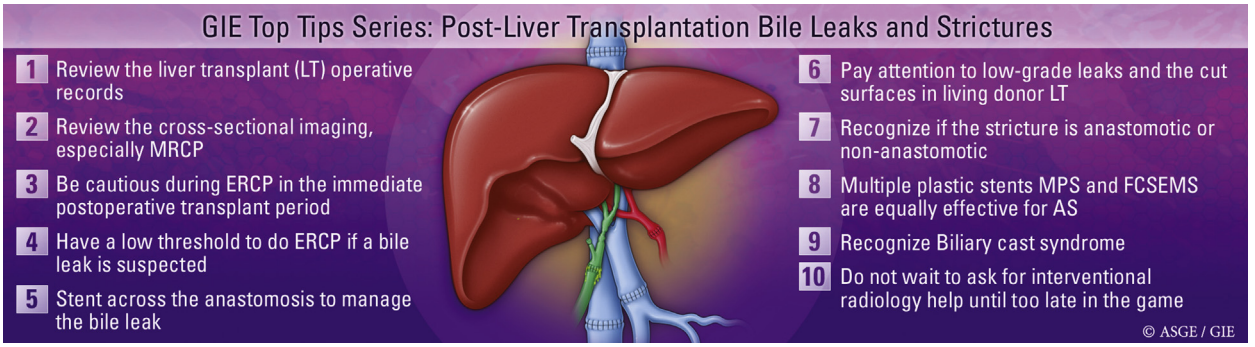
GRAPHICAL ABSTRACT



Many patients who have undergone a prior liver transplant will need an ERCP, and many need multiple ERCPs. Despite advances in surgical procedures and immunosuppressive therapy, adverse events after liver transplant remain common. Patients can present with a variety of problems including strictures, leaks, biliary cast syndrome, cholangitis, duct ischemia, and other problems. Many biliary endoscopists have little to no experience with these patients and may be understandably hesitant about performing ERCP when called on. In this Top Tips article, Thiruvengadam Muniraj lays out some extremely useful pearls of wisdom regarding how and when to approach some of the most common biliary problems after liver transplant.

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Abbreviations: AS, anastomotic stricture; FCSEMS, fully covered self-expandable metal stent; LDLT, living donor liver transplant; LT, liver transplant; NAS, nonanastomotic stricture.

DISCLOSURE: *Dr Muniraj is a consultant for Boston Scientific Corporation and Advisory Board member for the Assocation for Bariatric Endoscopy and American Society for Gastrointestinal Endoscopy*.

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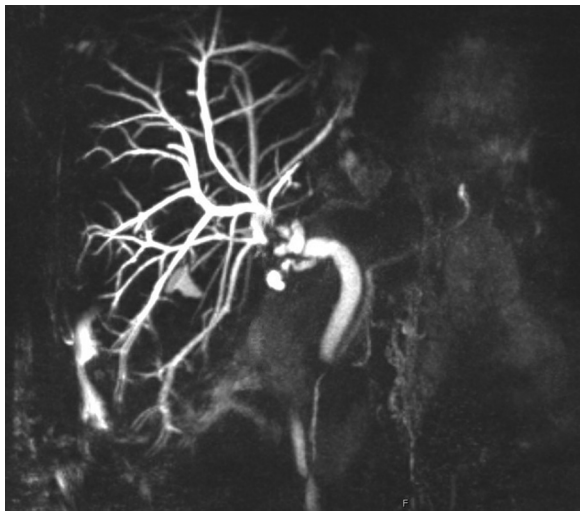

Figure 1. MRCP in the right lobe living donor liver transplant with biliary stricture at the right anterior and right posterior sectoral duct anastomosis to recipient left hepatic duct and right hepatic duct.

1. **Review the liver transplant (LT) operative records.** Proper knowledge of the postoperative anatomy of the surgical reconstruction during LT is crucial to the appropriate management of biliary leaks and strictures. The endoscopist should make all efforts to personally review the operative report. It is not uncommon to see an endoscopist struggling to cannulate the papilla, resulting in post-ERCP pancreatitis; meanwhile, the patient had actually undergone a Roux-en-Y hepaticojejunostomy. A clear understanding of the surgical anatomy will also

Figure 2. Living donor liver transplant with right hepatic lobe donation and stricture at the donor right anterior and right posterior sectoral duct anastomosis to recipient left hepatic duct and right hepatic duct (see pre-ERCP MRCP in Fig. 1).

Figure 3. Anastomotic bile leak managed with a fully covered self-expandable metal stent.

help the endoscopist plan ahead, choose the proper endoscope (duodenoscope, balloon-assisted enteroscope, or colonoscope), and prepare the right accessories. For example, because of the longer scope length and smaller working channel with enteroscopes, one must use specialized longer accessories and plastic stents of 5 or 7F rather than the conventionally used 10F stents. A colonoscope is necessary if a fully covered self-expandable metal stent (FCSEMS) is planned. Furthermore, the operative report helps the endoscopist understand the type of duct anastomosis because it differs among LT recipients depending on the type of donor

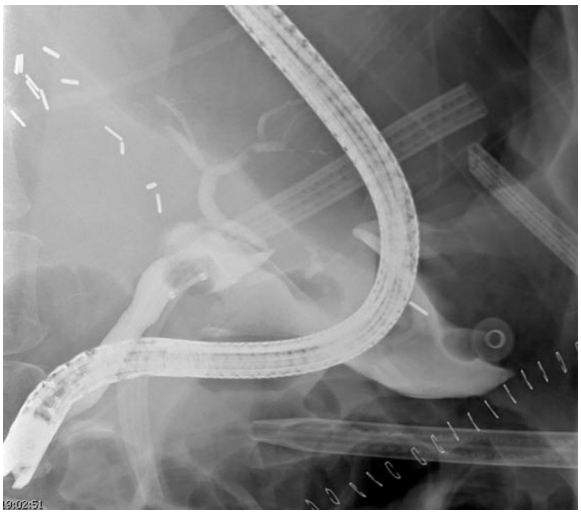

Figure 4. Donor cystic stump bile leak with duct–duct mismatch.

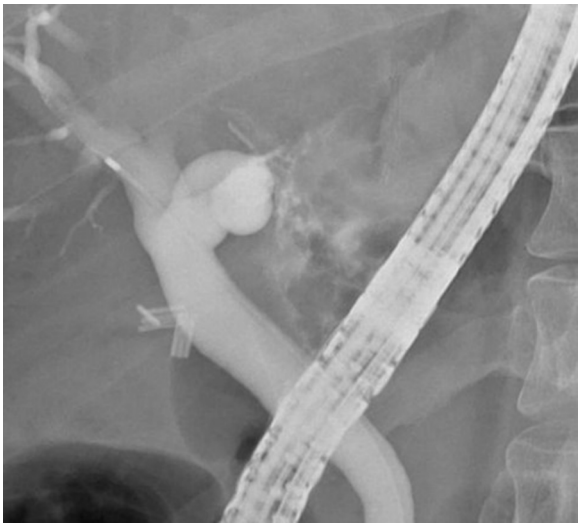

Figure 5. Cut surface leak in donor after left lobe donation.

livers: donation after circulatory death, living donor LT (LDLT), and split LT.[1]

2. **Review the cross-sectional imaging, especially MRCP.** Personally review all the available imaging, especially the MRCP. This provides a road map of the biliary system for the endoscopist to plan therapy in advance on which ducts to target (Figs. 1 and 2). In equivocal cases, after considering other etiologies for abnormal liver function tests, ask for MRCP to define whether the stricture is real or a duct–duct mismatch that may not need a stent. At this juncture, consult the transplant surgeon or refer to his or her operative notes wherein the knowledge regarding size mismatched ducts may provide additional help. Because MRCP cholangiogram may occasionally overcall a mild stricture, it is wise to look at the labs for cholestasis.

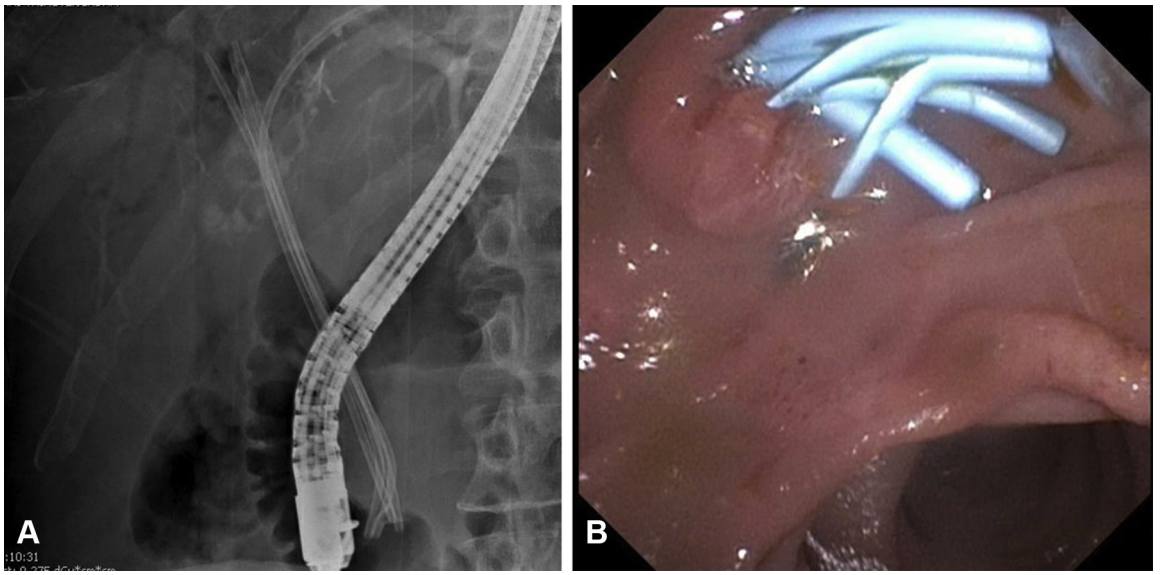

Figure 6. A, Multiple plastic stents placed through an anastomotic stricture. **B,** Multiple side-by-side plastic stents placed through an anastamotic stricture seen at the papilla.

Figure 7. Ischemic nonanastomotic strictures with biliary cast in donation after circulatory death transplantation.

3. **Be cautious during ERCP in the immediate postoperative transplant period.** Although some endoscopists advocate avoiding ERCP in the first 3 to 4 weeks after surgery, it can safely be done as early as 5 days postoperative; however, the utmost care must be taken to avoid rupturing the duct anastomosis. To avoid traction on the anastomosis, the endoscopist should refrain from sweeping the duct with a stone retrieval balloon. Before stenting, balloon dilations should be avoided entirely or performed using a small-caliber angioplasty balloon.[2] Because of immune suppression, providing periprocedural antibiotic coverage and continuing it postprocedure is vital.
4. **Have a low threshold to perform ERCP if a bile leak is suspected.** In a post-transplant setting, an undiagnosed sepsis, nonresolving ascites, or localized collection must prompt an aggressive evaluation of a bile leak. Even if MRCP, CT, hepatobiliary iminodiacetic acid (which relies on normal liver function and therefore may be falsely negative in early stages post-transplant), and peritoneal fluid analysis are equivocal, a strong clinical suspicion should warrant an ERCP. This is one of the few clinical situations where a diagnostic ERCP still remains the criterion standard.

Although it is common to have some bilious fluid from the surgical drain in the early post-LT period, a rising ascites bilirubin level and falling serum bilirubin level suggest a bile leak. In such situations, hepatobiliary iminodiacetic acid or MRCP are unnecessary, and an ERCP should be the next step. Bile leaks can still occur late after transplantation (early leak, <1 month; late leak, >1 month). Late bile leaks are often seen above a biliary stricture, particularly after liver biopsy sampling in a high-pressure duct**.**

5. **Stent across the anastomosis to manage the bile leak.** Post-transplant bile leaks are typically treated with biliary stenting. The goal is to direct the bile toward the duodenum. The gradient is not only at the papilla but also at the waist of the duct anastomosis when there is a mild stricture. To decrease the gradient for the leak to heal, it is critical to stent (starting with 7F) across the duct anastomosis and repeat ERCP in 6 weeks. Do not wait the usual 3 months to re-evaluate. An FCSEMS can be used in refractory leaks that persist after a second ERCP but still should be

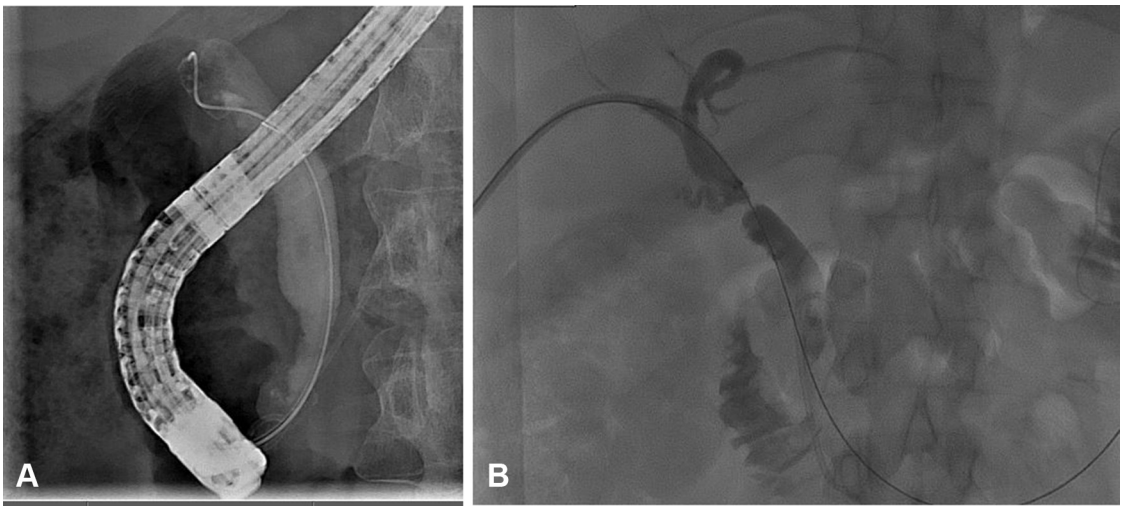

Figure 8. A, Very tight anastomotic stricture in which contrast or a guidewire is unable to pass. **B,** Very tight anastomotic stricture shown by percutaneous access with interventional radiology.

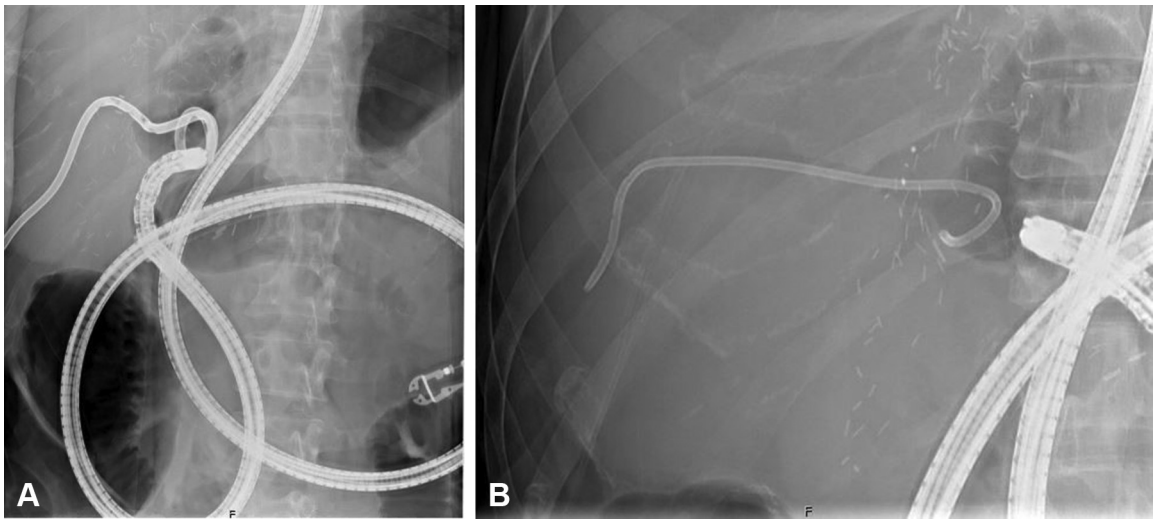

Figure 9. A, Roux-en-Y hepatojejunostomy with an external drain used to access the bile duct with ERCP. **B,** Roux-en-Y hepatojejunostomy with the external drain removed and internal ERCP stent placed.

followed up with ERCP sooner (in 4 months) because of sludge and secondary stricture formation (Fig. 3). Recognize that one-third of bile leak patients will develop a stricture.

6. **Pay attention to low-grade leaks and the cut surfaces in LDLT.** Low-grade leaks are often not evident during the initial cholangiogram. An occlusion cholangiogram should be done with a stone retrieval balloon at the level below the duct anastomosis, and the endoscopist must look carefully at the potential leak sites in a standard format (anastomotic site, cystic duct stumps at both recipient and donor, accessory bile ducts, cut surface of liver and intrahepatic bile ducts) (Fig. 4). If the leak is still not evident, check if the patient has a strong suction on the grenade with the drain tube closer to the leak site because the injected contrast may get sucked into the drain tube immediately rather than spilling. Reducing suction and slightly withdrawing the tube externally from the actual leak helps to diagnose and heal the leak. Minor cut surface leaks after liver resection usually settle down without intervention (Fig. 5).
7. **Recognize if the stricture is anastomotic or nonanastomotic.** Anastomotic stricture (AS) seen in MRCP is usually nonsignificant unless it is associated with clinical presentation of lab results (cholestasis or cholangitis) combined with strong evidence of intrahepatic biliary ductal dilation on imaging. In LDLT, anastomotic narrowing may not be a real stricture because the size of the donor right hepatic duct/left hepatic duct to recipient common bile duct is a mismatch. Diagnose a stricture only if the diameter of anastomosis

is <50% of the donor duct size. At the same time, post-transplant strictures, especially in LDLT, may not have prominent intrahepatic biliary dilation; therefore, if there is a clinical suspicion for a stricture (pruritus, rising alkaline phosphatase), perform a direct cholangiography with ERCP.

Nonanastomotic stricture (NAS) develops at least 5 mm or more proximal to the anastomosis in the donor ducts. NASs are typically diffuse and involve multiple sectoral/subsectoral ducts because of ischemia (rule out hepatic artery thrombosis by CT angiography) and have poor (40%) endoscopic therapy outcomes often requiring re-transplant. Hepatic artery thrombosis strictures often require more ERCPs, longer treatment, and bisectoral drainage. Late AS can present even around 24 months after the transplant, whereas NAS usually occurs in the first 4 to 6 months.

8. **Multiple plastic stents and FCSEMSs are equally effective for AS. Balloon dilation should be avoided in the early stage because of the risk of disruption of the anastomosis.**

   If the stricture is tight, start with a 7F stent, exchange it for a 10F stent in 2 to 3 months, and perform the dilation during the third ERCP after removing the 10F stent. Increasing the balloon dilation and adding the maximum number of side-by-side plastic stents (3-4 10F stents) should lead to a 97% success rate with stricture resolution (Fig. 6A and B).

   Multiple plastic stents and FCSEMS are now shown to be equally successful in AS.[3] Beware of the duct size because an oversized FCSEMS can cause secondary strictures. Because migration is the most critical risk along the course with the resolution of stricture, consider FCSEMSs with antimigratory fins, or leave a plastic double-pigtail stent within, or perform sphincterotomy and leave the FCSEMS intraductal above the major papilla. Even with FCSEMSs, repeat ERCP is recommended in 4 to 6 months because of sludge formation and risk of cholangitis.[4]

   Because of the small caliber of donor duct in LDLT, it may be necessary to start with a 5F stent and gradually upsize over several sessions.[5] Completion of stricture treatment should be considered when the anastomosis waist is fully obliterated during an occlusion cholangiogram after stent removal.

9. **Recognize biliary cast syndrome.** Any biliary obstruction can cause sludge and stone formation because of bile stasis. In NAS, multiple pigment stone casts are often seen within the intrahepatic ducts where ischemic strictures are present (Fig. 7). Cholangioscopy may be used to directly visualize, confirm, and flush the casts and clear the ducts.

10. **Do not wait to ask for interventional radiology help until it is too late in the game.** For many patients with Roux-en-Y hepaticojejunostomy, NASs, biliary cast syndrome, and a very tight AS, receiving a percutaneous transhepatic drainage sooner is helpful to preserve liver function and avoid the progression to biliary fibrosis/cirrhosis (Fig. 8A and B). Percutaneous transhepatic biliary drainage can sometimes be used as a rendezvous approach to internalize the external drains in patients whose biliary anastomosis can be accessed endoscopically after an interventional radiology intervention (Fig. 9A and B).

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